REMARKS

Support for the definition of n as 0 or 3 in Claim 1 is found in the specific compounds of the examples such as 4'-[2-(N,N-diethylamino)ethoxy]-6,7-methylenedioxy-5-hydroxy-flavone and 4'-[N-methyl-N-(3-methoxypropyl)amino)-5,6,7-trimethoxyflavone. Support for the definition of X^3 as OR^1 is found in the exemplified compounds having hydroxyl or methoxy substituents in the 4' position. Support for the other amendments to Claim 1 is found in the original language which has been modified to exclude certain of the options originally present.

New Claims 58 and 59 are directed to the use of compounds 1(d) and 10(b) described in the Examples.

Support for the additional compounds listed in Claim 11 is found as follows (using the line numbering shown in the PCT publication):

4'- (amino)- 5,7- dihydroxy-6-methoxy flavone: Compound 10b described on page 32;

4'- (amino)- 5,6,7-trimethoxy flavone: Compound 10a described on page 32;

4'-[N-methyl-N-(3-methoxypropyl)amino)-5,6,7-trimethoxyflavone: page 34 lines 21 – 24;

4'-[N,N-di(2-hydroxyethyl)-amino)-5,7-dihydroxy-6-methoxyflavone: page 34 lines 26 – 32;

4'-(2-hydroxyethylamino)-5,7-dihydroxy-6-methoxyflavone: page 34 lines 26–32;

4'-(2-methanesulfonatoethylamino)-5,7-dihydroxy-6-methoxyflavone: page 35 lines 5 – 15;

4'-[2-(N,N-diethylamino)ethylamino]-5,7-dihydroxy-6-methoxyflavone: page 35 lines 17 – 21;

4'-[2-(N,N-diethylamino)ethoxy]-6,7-methylenedioxy-5-hydroxy-flavone: page 35 lines 32 -35; and

4'-(2,3-dihydroxy-propyloxy)-5,6,7-trimethoxyflavone: page 36 lines 5-10.

The method of use claims have been limited to treatment of conditions for which specific information has been set out in the application namely overproduction of TNF-α, overproduction of superoxide and organ damage, in particular lung, liver and kidney damage. The experimental results set out in the Figures 1 -6 and 9 were obtained using baicalein sulfate. Those in Figs 7 and 8 were obtained using baicalein These data provide reasonable support for accepting the credibility of the use of this compound for treatment of the conditions now specified. Contrary to the examiner's understanding, the Figures contain not only *in vivo* information but also

Effects on mean arterial pressure in LPS-treated rats (Fig 1),

Effects on heart rates of LPS-treated rats (Fig 2),

TNF-α levels in plasma of LPS-treated rats (Figs 3 and 7),

Superoxide anion production in LPS-treated rats (Figs 4 and 8)

Effects on SGPT levels in LPS-treated rats (Fig 5),

Effects on SGOT levels in LPS-treated rats (Fig 6), and

histological studies showing the effects of baicalein sulfate on LPS-induced damage on rat lung tissue.

Elevated SGOT and SGPT levels are indicative of liver damage which is a common diagnostic biomarker used clinically

Submitted herewith are additional *in vitro* data showing the effects of other compounds falling within the present invention on TNF-α production in U937 cells. These again support the credibility of the invention claimed. The compounds specified in the claims are all analogs of baicalein and its sulfate and the compounds shown in the data submitted herewith. One skilled in the art would accept that they have the use described and would be able to put them into practice for that use.

We now turn to the issues based on the prior art.

So far as the method of treatment claims are concerned, Cassels describes anxiolytic uses and Hander refers to isoflavones in general as having antiangiogenic, antihemolytic, antiischemic, antileukemic, antimitogenic, antimutagenic, antioxidant, fungicidal, pesticidal, MAO-inhibition, phytoalexin, and tyrosine kinase inhibition activities and anticancer effects. Neither of these therefore points in any way towards the methods of the present claims.

So far as Lee is concerned, this does teach the use of flavanoid compounds as inhibition expression of iNOS, cyclooxygenase, and angiotensin. There is, however, no suggestion that the compounds are of use in treating organ damage.

The definitions of the compound claims have been amended with the objective of avoiding prior art compounds. There is no reason why one skilled in the art would have thought to modify the prior art compounds to produce those now claimed, having the properties that they do in treating damage to specific organs. The compounds defined in Claim 1 are novel and there is no report that 4'-hydroxy or 4-methoxy baicalein analogs possesses the same activity as we documented in this application.

Regarding the inventors, Dr. Mao-Hsiung Yen is the inventor for flavone derivatives as shown in US applications 60/420,306 and 60/453,771. Edwin S. Wu is the inventor for expanding the flavone analogs to isoflavone and 2,3-diphenylchromone derivatives and also a contributor to the design and synthesis of 4'-substituted derivatives as shown in the PCT applications.

In view of the foregoing, it is submitted that this application is in condition for allowance and an early action to this end is respectfully solicited.

Respectfully submitted,

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